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Bhatia, Tanya
Davis, Theodore
Lovasco, Lindsay

<120> Recombinant Type II Restriction Endonucleases, MmeI And Other Related Endonucleases And Methods For Producing The Same

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<151> 2002-07-12

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65                  70                  75                  80

Met Lys Ser Arg Gly Lys Asp Leu Asp Lys Ala Tyr Asp Gln Ala Leu
                85                  90                  95

Asp Tyr Phe Ser Gly Ile Ala Glu Arg Asp Leu Pro Arg Tyr Val Leu
            100                 105                 110

Val Cys Asp Phe Gln Arg Phe Arg Leu Thr Asp Leu Ile Thr Lys Glu
        115                 120                 125

Ser Val Glu Phe Leu Leu Lys Asp Leu Tyr Gln Asn Val Arg Ser Phe
    130                 135                 140

Gly Phe Ile Ala Gly Tyr Gln Thr Gln Val Ile Lys Pro Gln Asp Pro
145                 150                 155                 160

Ile Asn Ile Lys Ala Ala Glu Arg Met Gly Lys Leu His Asp Thr Leu
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Lys Leu Val Gly Tyr Glu Gly His Ala Leu Glu Leu Tyr Leu Val Arg
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Leu Phe Gln Glu Tyr Ile Glu Thr Lys Thr Leu Glu Asp Gly Ser Asp
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Leu Ala His His Ile Asn Thr Leu Phe Tyr Val Leu Asn Thr Pro Glu
225                 230                 235                 240

Gln Lys Arg Leu Lys Asn Leu Asp Glu His Leu Ala Ala Phe Pro Tyr
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Ile Asn Gly Lys Leu Phe Glu Glu Pro Leu Pro Pro Ala Gln Phe Asp
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Lys Ala Met Arg Glu Ala Leu Leu Asp Leu Cys Ser Leu Asp Trp Ser
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            340                 345                 350

Lys Leu Arg Gly Leu Thr Phe Phe Asp Pro Ala Cys Gly Cys Gly Asn
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Leu Arg Gly Leu His Arg Gly Gly Gln Gln Val Leu Asp Ile Glu His
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Leu Ile Gln Ile Asn Val Asp Gln Phe Phe Gly Ile Glu Ile Glu Glu
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Met Asn Met Lys Ile Ser Asp Glu Phe Gly Asn Tyr Phe Ala Arg Ile
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Pro Leu Lys Ser Thr Pro His Ile Leu Asn Ala Asn Ala Leu Gln Ile
    450                 455                 460

Asp Trp Asn Asp Val Leu Glu Ala Lys Lys Cys Cys Phe Ile Leu Gly
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Asn Pro Pro Phe Val Gly Lys Ser Lys Gln Thr Pro Gly Gln Lys Ala
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Asp Leu Leu Ser Val Phe Gly Asn Leu Lys Ser Ala Ser Asp Leu Asp
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Leu Val Ala Ala Trp Tyr Pro Lys Ala Ala His Tyr Ile Gln Thr Asn
        515                 520                 525

Ala Asn Ile Arg Cys Ala Phe Val Ser Thr Asn Ser Ile Thr Gln Gly
    530                 535                 540

Glu Gln Val Ser Leu Leu Trp Pro Leu Leu Leu Ser Leu Gly Ile Lys
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Ile Asn Phe Ala His Arg Thr Phe Ser Trp Thr Asn Glu Ala Ser Gly
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Val Ala Ala Val His Cys Val Ile Ile Gly Phe Gly Leu Lys Asp Ser
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Asp Glu Lys Ile Ile Tyr Glu Tyr Glu Ser Ile Asn Gly Glu Pro Leu
595 600 605

Ala Ile Lys Ala Lys Asn Ile Asn Pro Tyr Leu Arg Asp Gly Val Asp
610 615 620

Val Ile Ala Cys Lys Arg Gln Gln Pro Ile Ser Lys Leu Pro Ser Met
625 630 635 640

Arg Tyr Gly Asn Lys Pro Thr Asp Asp Gly Asn Phe Leu Phe Thr Asp
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Glu Glu Lys Asn Gln Phe Ile Thr Asn Glu Pro Ser Ser Glu Lys Tyr
660 665 670

Phe Arg Arg Phe Val Gly Gly Asp Glu Phe Ile Asn Asn Thr Ser Arg
675 680 685

Trp Cys Leu Trp Leu Asp Gly Ala Asp Ile Ser Glu Ile Arg Ala Met
690 695 700

Pro Leu Val Leu Ala Arg Ile Lys Lys Val Gln Glu Phe Arg Leu Lys
705 710 715 720

Ser Ser Ala Lys Pro Thr Arg Gln Ser Ala Ser Thr Pro Met Lys Phe
725 730 735

Phe Tyr Ile Ser Gln Pro Asp Thr Asp Tyr Leu Leu Ile Pro Glu Thr
740 745 750

Ser Ser Glu Asn Arg Gln Phe Ile Pro Ile Gly Phe Val Asp Arg Asn
755 760 765

Val Ile Ser Ser Asn Ala Thr Tyr His Ile Pro Ser Ala Glu Pro Leu
770 775 780

Ile Phe Gly Leu Leu Ser Ser Thr Met His Asn Cys Trp Met Arg Asn
785 790 795 800

Val Gly Gly Arg Leu Glu Ser Arg Tyr Arg Tyr Ser Ala Ser Leu Val
805 810 815

Tyr Asn Thr Phe Pro Trp Ile Gln Pro Asn Glu Lys Gln Ser Lys Ala
820 825 830

Ile Glu Glu Ala Ala Phe Ala Ile Leu Lys Ala Arg Ser Asn Tyr Pro
835 840 845

Asn Glu Ser Leu Ala Gly Leu Tyr Asp Pro Lys Thr Met Pro Ser Glu
850 855 860

Leu Leu Lys Ala His Gln Lys Leu Asp Lys Ala Val Asp Ser Val Tyr
865 870 875 880

Gly Phe Lys Gly Pro Asn Thr Glu Ile Ala Arg Ile Ala Phe Leu Phe
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35 40 45

Thr Tyr Glu Lys Asp Val Gln Val Lys Ala Asp Gly Lys Val Thr Thr
50 55 60

Arg Arg Ile Asp Gly Tyr Ile Pro Ser Thr Lys Ile Met Val Glu Met
65 70 75 80

Lys Gly Lys Asn Ile Lys Asp Leu Ser Lys Pro Ile Thr Gln Ser Gly

85 90 95

Gly Asp Glu Leu Thr Pro Phe Glu Gln Ala Lys Arg Tyr Ala Asn Phe
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Leu Pro Asn Ser Glu Gln Pro Arg Trp Ile Leu Val Ser Asn Phe Asn
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Glu Ile Asp Ile His Asp Met Glu Arg Pro Leu Asp Glu Pro Lys Val
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Ile Lys Leu Glu Asp Leu Pro Lys Lys Val Lys Ser Leu Glu Phe Met
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Val Asp Ala Asn Gln Gln Gln Val Ile Asp Glu Lys Gln Leu Ser Val
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Asp Ala Gly Asn Leu Val Ala Lys Ile Tyr Asn Glu Leu Thr Asn Ala
180 185 190

Tyr Ala Ala Gly Arg Gly Ile Asp Val Asn Glu Pro Arg Ile Gln Arg
195 200 205

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Asp Ser Asn Leu Phe Gly Lys Glu Asp Ile Phe Gln Ala Phe Ile Glu
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Arg Arg Glu Pro Arg Asp Ile Arg Arg Asp Leu Ser Glu Leu Phe Lys
245 250 255

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Val Ile Ile Pro Gln Phe Thr Asp Glu Leu Lys Arg Leu Ile Val Glu
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Asp Ala Gly Arg Gly Phe Asp Trp Ser Gly Ile Ser Pro Thr Ile Phe
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Gly Ala Val Phe Glu Ser Thr Leu Asn Pro Glu Thr Arg Arg Ser Gly
325 330 335

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Gly Asn Arg Arg Gln Arg Val Thr Arg Ala Lys Ala Phe Arg Asp Lys
    370                 375                 380

Leu Gly Lys Leu Lys Phe Phe Asp Pro Ala Cys Gly Ser Gly Asn Phe
385                 390                 395                 400

Leu Thr Glu Thr Tyr Leu Ser Leu Arg Lys Met Glu Asn Glu Cys Leu
                405                 410                 415

Arg Ile Ile Val Gly Asn Gln Gly Ala Leu Ala Leu Thr Asp Glu Ser
            420                 425                 430

Glu Pro Lys Val Lys Ile Gln Asn Phe Tyr Gly Ile Glu Ile Asn Asp
        435                 440                 445

Phe Ala Val Ser Val Ala Arg Thr Ala Met Trp Ile Ala Glu Ser Gln
    450                 455                 460

Met Trp Glu Gln Thr Lys Asp Ile Thr Phe Ala Asn Lys Asp Phe Leu
465                 470                 475                 480

Pro Leu Asp Ser Asn Asp Ser Ile Tyr Glu Gly Asn Ala Leu Arg Met
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Asp Trp Asn Asp Ile Val Lys Pro Tyr Glu Leu Asp Tyr Ile Met Gly
            500                 505                 510

Asn Pro Pro Phe Val Gly Tyr Ser Leu Gln Thr Lys Glu Gln Lys Gln
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Asp Ile Lys Gln Glu Phe Phe Lys Tyr Thr Asp Lys Tyr Gly Lys Phe
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Asp Tyr Val Ser Gly Trp Tyr Ile Lys Gly Ala Lys Tyr Ile Gln Asn
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Ser Thr Ile Lys Val Gly Phe Val Ser Thr Asp Ser Ile Ile Gln Gly
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Glu Gln Ala Pro Glu Ile Trp Lys Val Leu Phe Asn Asp Phe His Ile
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Phe Ile Asn Tyr Gly Tyr Arg Ser Phe Glu Trp Asn Asn Glu Ala Ala
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Asp Lys Asn Pro Thr Ile Tyr Asp Glu Gln Lys Ile Ile Ser Ala Lys
625                 630                 635                 640

His Ile Asn Gln Tyr Met Tyr Asp Ser Asp Asn Ile Phe Ile Asp Thr
                645                 650                 655

Thr Arg Lys Tyr Ile Glu Ala Met Pro Lys Met Lys Thr Gly Asn Arg
            660                 665                 670

Pro Ala Asp Gly Gly Ala Leu Ile Leu Ser Pro Lys Glu Ala Lys Glu
        675                 680                 685

Leu Val Asn Glu Glu Pro Gln Ser Lys Gln Phe Ile Lys Lys Leu Thr
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Gly Ser Lys Glu Phe Ile Thr Gly Lys Tyr Arg Tyr Cys Leu Trp Leu
705                 710                 715                 720

Val Asn Val Thr Pro Lys Gln Leu Arg Ser Met Pro Leu Val Leu Lys
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Arg Val Glu Gln Cys Lys Glu Asn Arg Leu Ser Gly Ala Pro Asp Arg
            740                 745                 750

Gln Lys Leu Ala Ala Thr Pro His Leu Phe Arg Glu Gln Met Asn Pro
        755                 760                 765

Asp Asn Tyr Met Ile Val Pro Leu Val Thr Gly Cys Arg Arg Lys Tyr
    770                 775                 780

Val Pro Phe Gly Tyr Leu Gly Asn Asp Ile Ile Pro Thr Asn Leu Ala
785                 790                 795                 800

Thr Ile Ile Pro Glu Ala Asp His Tyr Ala Phe Gly Val Leu Glu Ser
                805                 810                 815

Ile Val His Met Ala Trp Met Arg Val Val Ala Gly Arg Lys Gly Thr
            820                 825                 830

Ser Tyr Arg Tyr Ser Lys Asn Leu Val Tyr Thr Asn Phe Pro Trp Pro
        835                 840                 845
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Val Val Asp Ile Asn Gln Lys Glu Lys Ile Thr Ile Thr Ala Gln Asp
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Ile Leu Asn Ala Arg Asn Leu Tyr Pro Asp Ser Ser Leu Ala Asp Leu
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Tyr Asp Pro Leu Thr Met Pro Ile Glu Leu Arg Lys Ala His Glu Ala
                885                 890                 895

Asn Asp Lys Ala Val Leu Lys Ala Tyr Gly Leu Lys Pro Ser Ala Thr
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Ile Val Gly Phe Ser Thr Lys Glu Asp Lys Asn Pro Thr Ile Tyr Asp
        35                  40                  45

Ser Ser Asn Ile Ser His Cys Lys Asn Ile Asn Gly Tyr Leu Phe Asp
    50                  55                  60

Gly Asn Asn Ile Phe Val Thr Asn Arg Pro Ala Pro Leu Ser Asn Val
65                  70                  75                  80

Pro Arg Met His Asn Gly Cys Lys Leu Leu Asp Gly Gly Phe Tyr Thr
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Leu Thr Ser Gln Glu Arg Lys Glu Ala Ile Ser Lys Asp Pro Tyr Ala
            100                 105                 110
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Thr Ala Arg Tyr Cys Ile Trp Leu Lys Asp Ala Asn Pro Lys Asp Ile
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His Gln Ser Pro Phe Ile Leu Asp Arg Ile Asn Lys Val Ala Glu Phe
145                 150                 155                 160

Arg Ser Gln Gln Lys Ser Lys Asp Thr Gln Lys Tyr Ala Lys Arg Pro
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Met Leu Pro Thr Arg Leu Ala Tyr Tyr Ser His Asp Glu His Thr Asp
            180                 185                 190

Met Leu Ile Val Pro Ala Thr Ser Ser Gln Arg Arg Glu Tyr Leu Pro
        195                 200                 205

Ile Gly Tyr Val Ser Glu Lys Asn Ile Val Ser Tyr Ser Leu Met Leu
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His Tyr Ile Trp Leu Lys Asn Phe Cys Gly Arg Leu Lys Ser Asp Tyr
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Arg Tyr Ser Asn Thr Ile Ile Tyr Asn Asn Phe Pro Trp Pro Thr Val
            260                 265                 270

Gly Asp Lys Gln Glu Gln Asn Ile Ser Glu Thr Ala Gln Gly Ile Leu
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Asn Thr Arg Lys Leu Tyr Pro Asp Ser Ser Leu Ala Asp Leu Tyr Asp
    290                 295                 300

Pro Leu Thr Met Pro Val Glu Leu Arg Lys Ala His Glu Ala Asn Asp
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Met Ala Leu Ser Trp Asn Glu Ile Arg Arg Lys Ala Ile Glu Phe Ser
1               5                  10                  15

Lys Arg Trp Glu Asp Ala Ser Asp Glu Asn Ser Gln Ala Lys Pro Phe
            20                  25                  30

Leu Ile Asp Phe Phe Glu Val Phe Gly Ile Thr Asn Lys Arg Val Ala
        35                  40                  45

Thr Phe Glu His Ala Val Lys Lys Phe Ala Lys Ala His Lys Glu Gln
    50                  55                  60

Ser Arg Gly Phe Val Asp Leu Phe Trp Pro Gly Ile Leu Leu Ile Glu
65                  70                  75                  80

Met Lys Ser Arg Gly Lys Asp Leu Asp Lys Ala Tyr Asp Gln Ala Leu
                85                  90                  95

Asp Tyr Phe Ser Gly Ile Ala Glu Arg Asp Leu Pro Arg Tyr Val Leu
            100                 105                 110

Val Cys Asp Phe Gln Arg Phe Arg Leu Thr Asp Leu Ile Thr Lys Glu
        115                 120                 125

Ser Val Glu Phe Leu Leu Lys Asp Leu Tyr Gln Asn Val Arg Ser Phe
    130                 135                 140

Gly Phe Ile Ala Gly Tyr Gln Thr Gln Val Ile Lys Pro Gln Asp Pro
145                 150                 155                 160

Ile Asn Ile Lys Ala Ala Glu Arg Met Gly Lys Leu His Asp Thr Leu
                165                 170                 175

Lys Leu Val Gly Tyr Glu Gly His Ala Leu Glu Leu Tyr Leu Val Arg
            180                 185                 190

Leu Leu Phe Cys Leu Phe Ala Glu Asp Thr Thr Ile Phe Glu Lys Ser
        195                 200                 205
```

```
Leu Phe Gln Glu Tyr Ile Glu Thr Lys Thr Leu Glu Asp Gly Ser Asp
    210                 215                 220

Leu Ala His His Ile Asn Thr Leu Phe Tyr Val Leu Asn Thr Pro Glu
225                 230                 235                 240

Gln Lys Arg Leu Lys Asn Leu Asp Glu His Leu Ala Ala Phe Pro Tyr
                245                 250                 255

Ile Asn Gly Lys Leu Phe Glu Glu Pro Leu Pro Pro Ala Gln Phe Asp
            260                 265                 270

Lys Ala Met Arg Glu Ala Leu Leu Asp Leu Cys Ser Leu Asp Trp Ser
        275                 280                 285

Arg Ile Ser Pro Ala Ile Phe Gly Ser Leu Phe Gln Ser Ile Met Asp
    290                 295                 300

Ala Lys Lys Arg Arg Asn Leu Gly Ala His Tyr Thr Ser Glu Ala Asn
305                 310                 315                 320

Ile Leu Lys Leu Ile Lys Pro Leu Phe Leu Asp Glu Leu Trp Val Glu
                325                 330                 335

Phe Glu Lys Val Lys Asn Asn Lys Asn Lys Leu Leu Ala Phe His Lys
            340                 345                 350

Lys Leu Arg Gly Leu Thr Phe Phe Asp Pro Ala Cys Gly Cys Gly Asn
        355                 360                 365

Phe Leu Val Ile Thr Tyr Arg Glu Leu Arg Leu Leu Glu Ile Glu Val
    370                 375                 380

Leu Arg Gly Leu His Arg Gly Gly Gln Gln Val Leu Asp Ile Glu His
385                 390                 395                 400

Leu Ile Gln Ile Asn Val Asp Gln Phe Phe Gly Ile Glu Ile Glu Glu
                405                 410                 415

Phe Pro Ala Gln Ile Ala Gln Val Ala Leu Trp Leu Thr Asp His Gln
            420                 425                 430

Met Asn Met Lys Ile Ser Asp Glu Phe Gly Asn Tyr Phe Ala Arg Ile
        435                 440                 445

Pro Leu Lys Ser Thr Pro His Ile Leu Asn Ala Asn Ala Leu Gln Ile
    450                 455                 460
```

```
Asp Trp Asn Asp Val Leu Glu Ala Lys Lys Cys Cys Phe Ile Leu Gly
465                 470                 475                 480

Asn Pro Pro Phe Val Gly Lys Ser Lys Gln Thr Pro Gly Gln Lys Ala
                485                 490                 495

Asp Leu Leu Ser Val Phe Gly Asn Leu Lys Ser Ala Ser Asp Leu Asp
            500                 505                 510

Leu Val Ala Ala Trp Tyr Pro Lys Ala Ala His Tyr Ile Gln Thr Asn
        515                 520                 525

Ala Asn Ile Arg Cys Ala Phe Val Ser Thr Asn Ser Ile Thr Gln Gly
    530                 535                 540

Glu Gln Val Ser Leu Leu Trp Pro Leu Leu Leu Ser Leu Gly Ile Lys
545                 550                 555                 560

Ile Asn Phe Ala His Arg Thr Phe Ser Trp Thr Asn Glu Ala Ser Gly
                565                 570                 575

Val Ala Ala Val His Cys Val Ile Ile Gly Phe Gly Leu Lys Asp Ser
            580                 585                 590

Asp Glu Lys Ile Ile Tyr Glu Tyr Glu Ser Ile Asn Gly Glu Pro Leu
        595                 600                 605

Ala Ile Lys Ala Lys Asn Ile Asn Pro Tyr Leu Arg Asp Gly Val Asp
    610                 615                 620

Val Ile Ala Cys Lys Arg Gln Gln Pro Ile Ser Lys Leu Pro Ser Met
625                 630                 635                 640

Arg Tyr Gly Asn Lys Pro Thr Asp Asp Gly Asn Phe Leu Phe Thr Asp
                645                 650                 655

Glu Glu Lys Asn Gln Phe Ile Thr Asn Glu Pro Ser Ser Glu Lys Tyr
            660                 665                 670

Phe Arg Arg Phe Val Gly Gly Asp Glu Phe Ile Asn Asn Thr Ser Arg
        675                 680                 685

Trp Cys Leu Trp Leu Asp Gly Ala Asp Ile Ser Glu Ile Arg Ala Met
    690                 695                 700

Pro Leu Val Leu Ala Arg Ile Lys Lys Val Gln Glu Phe Arg Leu Lys
```

705 710 715 720

Ser Ser Ala Lys Pro Thr Arg Gln Ser Ala Ser Thr Pro Met Lys Phe
725 730 735

Phe Tyr Ile Ser Gln Pro Asp Thr Asp Tyr Leu Leu Ile Pro Glu Thr
740 745 750

Ser Ser Glu Asn Arg Gln Phe Ile Pro Ile Gly Phe Val Asp Arg Asn
755 760 765

Val Ile Ser Ser Asn Ala Thr Tyr His Ile Pro Ser Ala Glu Pro Leu
770 775 780

Ile Phe Gly Leu Leu Ser Ser Thr Met His Asn Cys Trp Met Arg Asn
785 790 795 800

Val Gly Gly Arg Leu Glu Ser Arg Tyr Arg Tyr Ser Ala Ser Leu Val
805 810 815

Tyr Asn Thr Phe Pro Trp Ile Gln Pro Asn Glu Lys Gln Ser Lys Ala
820 825 830

Ile Glu Glu Ala Ala Phe Ala Ile Leu Lys Ala Arg Ser Asn Tyr Pro
835 840 845

Asn Glu Ser Leu Ala Gly Leu Tyr Asp Pro Lys Thr Met Pro Ser Glu
850 855 860

Leu Leu Lys Ala His Gln Lys Leu Asp Lys Ala Val Asp Ser Val Tyr
865 870 875 880

Gly Phe Lys Gly Pro Asn Thr Glu Ile Ala Arg Ile Ala Phe Leu Phe
885 890 895

Glu Thr Tyr Gln Lys Met Thr Ser Leu Leu Pro Pro Glu Lys Glu Ile
900 905 910

Lys Lys Ser Lys Gly Lys Asn
915

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Met Lys Thr Leu Leu Gln Leu Gln Thr Ala Ala Gln Asn Phe Ala Ala
1               5                  10                  15

Tyr Tyr Lys Asp Gln Thr Asp Glu Arg Arg Glu Lys Asp Thr Phe Asn
            20                  25                  30

Glu Phe Phe Ala Ile Phe Gly Ile Asp Arg Lys Asn Val Ala His Phe
        35                  40                  45

Glu Tyr Pro Val Lys Asp Pro Ala Asp Asn Thr Gln Phe Val Asp Ile
    50                  55                  60

Phe Trp Glu Gly Ile Phe Leu Ala Glu His Lys Ser Ala Asn Lys Asn
65                  70                  75                  80

Leu Thr Lys Ala Lys Glu Gln Ala Glu Arg Tyr Leu Gln Glu Ile Gly
                85                  90                  95

Arg Thr Lys Pro Ser Ala Leu Pro Glu Tyr Tyr Ala Val Ser Asp Phe
            100                 105                 110

Ala His Phe His Leu Tyr Arg Arg Val Pro Glu Glu Gly Ala Glu Asn
        115                 120                 125

Gln Trp Gln Phe Pro Leu Glu Glu Leu Pro Glu Tyr Ile Thr Arg Gly
    130                 135                 140

Val Phe Asp Phe Met Phe Gly Ile Glu Ala Lys Val Arg Gln Ile Gln
145                 150                 155                 160

Glu Glu Ala Asn Ile Gln Ala Ala Ala Thr Ile Gly Arg Leu His Asp
                165                 170                 175

Ala Leu Lys Glu Glu Gly Ile Tyr Glu Glu His Glu Leu Arg Leu Phe
            180                 185                 190

Ile Thr Arg Leu Leu Phe Leu Phe Phe Ala Asp Asp Ser Ala Val Phe
        195                 200                 205

Arg Arg Asn Tyr Leu Phe Gln Asp Phe Leu Glu Asn Cys Lys Glu Ala
    210                 215                 220

Asp Thr Leu Gly Asp Lys Leu Asn Gln Leu Phe Glu Phe Leu Asn Thr
225                 230                 235                 240

Pro Asp Gln Lys Arg Ser Lys Thr Gln Ser Glu Lys Phe Lys Gly Phe
```

245 250 255

Glu Tyr Val Asn Gly Gly Leu Phe Lys Glu Arg Leu Arg Thr Phe Asp
260 265 270

Phe Thr Ala Lys Gln His Arg Ala Leu Ile Asp Cys Gly Asn Phe Asp
275 280 285

Trp Arg Asn Ile Ser Pro Glu Ile Phe Gly Thr Leu Phe Gln Ser Val
290 295 300

Met Asp Ala Gln Glu Arg Arg Glu Ala Gly Ala His Tyr Thr Glu Ala
305 310 315 320

Ala Asn Ile Asp Lys Val Ile Asn Gly Leu Phe Leu Glu Asn Leu Arg
325 330 335

Ala Glu Phe Glu Ala Val Lys Ala Leu Lys Arg Asp Lys Ala Lys Lys
340 345 350

Leu Ala Ala Phe Tyr Gln Lys Ile Gln Asn Leu Gln Phe Leu Asp Pro
355 360 365

Ala Cys Gly Cys Gly Asn Phe Leu Ile Val Ala Tyr Asp Arg Ile Arg
370 375 380

Ala Leu Glu Asp Asp Ile Ile Ala Glu Ala Leu Lys Asp Lys Ala Asp
385 390 395 400

Gly Leu Phe Asp Ser Pro Ser Val Gln Cys Arg Leu Lys Gln Phe His
405 410 415

Gly Ile Glu Ile Asp Glu Phe Ala Val Leu Ile Ala Arg Thr Ala Met
420 425 430

Trp Leu Lys Asn His Gln Cys Asn Ile Arg Thr Gln Ile Arg Phe Asp
435 440 445

Gly Glu Val Ala Cys His Thr Leu Pro Leu Glu Asp Ala Ala Glu Ile
450 455 460

Ile His Ala Asn Ser Leu Arg Thr Pro Trp Gln Ala Ala Asp Tyr Ile
465 470 475 480

Phe Gly Asn Pro Pro Phe Ile Gly Ser Thr Tyr Gln Thr Lys Glu Gln
485 490 495

```
Lys Asn Asp Leu Glu Ser Ile Cys Gly His Ile Lys Gly Tyr Gly Leu
            500                 505                 510

Leu Asp Tyr Val Cys Asn Trp Tyr Val Lys Ala Ala Gly Ile Met Ala
        515                 520                 525

Gln His Pro Gln Val Gln Thr Ala Phe Val Ser Thr Asn Ser Ile Cys
    530                 535                 540

Gln Gly Gln Gln Val Glu Ile Leu Trp Gly Ser Leu Leu Asn Gln Gly
545                 550                 555                 560

Ile Glu Ile His Phe Ala His Arg Thr Phe Gln Trp Thr Ser Gln Ala
                565                 570                 575

Ala Gly Lys Ala Ala Val His Cys Ile Ile Val Gly Phe Arg Gln Lys
            580                 585                 590

Pro Pro Met Pro Ser Glu Lys Thr Leu Tyr Asp Tyr Pro Asp Ile Lys
        595                 600                 605

Gly Glu Pro Glu Lys His Ala Val Ala Asn Ile Asn Pro Tyr Leu Ile
    610                 615                 620

Asp Ala Pro Asp Leu Ile Ile Ala Lys Arg Ser Arg Pro Ile His Cys
625                 630                 635                 640

Glu Pro Asp Met Val Asn Gly Ser Lys Pro Thr Glu Gly Gly Asn Leu
                645                 650                 655

Ile Leu Ser Thr Ala Glu Lys Asp Ala Leu Ile Ala Ala Glu Pro Leu
            660                 665                 670

Ala Glu Gln Tyr Ile Arg Pro Phe Ile Gly Ala Asp Glu Phe Leu Asn
        675                 680                 685

Gly Lys Thr Arg Trp Cys Leu Trp Phe His Gly Val Ser Asp Val Lys
    690                 695                 700

Arg Asn His Asp Leu Lys Gln Met Pro Gln Val Gln Ala Arg Ile Gln
705                 710                 715                 720

Ala Val Lys Thr Met Arg Glu Ala Ser Ser Asp Lys Gln Thr Gln Lys
                725                 730                 735

Asp Ala Ala Thr Pro Trp Leu Phe Gln Lys Ile Arg Gln Pro Ser Asp
            740                 745                 750
```

```
Gly Asn Tyr Leu Ile Ile Pro Ser Val Ser Ser Glu Ser Arg Arg Phe
        755                 760                 765

Ile Pro Ile Gly Tyr Leu Ser Phe Glu Thr Val Val Ser Asn Leu Ala
    770                 775                 780

Phe Ile Leu Pro Asn Ala Thr Leu Tyr His Phe Gly Ile Leu Ser Ser
785                 790                 795                 800

Thr Met His Asn Ala Phe Met Arg Thr Val Ala Gly Arg Leu Lys Ser
                805                 810                 815

Asp Tyr Arg Tyr Ser Asn Thr Val Val Tyr Asn Asn Phe Pro Phe Pro
            820                 825                 830

Glu Ser Cys Arg Leu Pro Ser Glu Asn Asp Arg Pro Asp Pro Leu Arg
        835                 840                 845

Ala Ala Val Glu Ala Ala Ala Gln Thr Val Leu Asp Ala Arg Gly Gln
    850                 855                 860

Tyr Arg Arg Glu Ala Gln Glu Ala Gly Leu Pro Glu Pro Thr Leu Ala
865                 870                 875                 880

Glu Leu Tyr Ala Pro Asp Ala Gly Tyr Thr Ala Leu Asp Lys Ala His
                885                 890                 895

Ala Thr Leu Asp Lys Ala Val Asp Lys Ala Tyr Gly Tyr Lys Thr Gly
            900                 905                 910

Lys Asn Thr Asp Asp Glu Ala Glu Arg Val Ala Phe Leu Phe Glu Leu
        915                 920                 925

Tyr Arg Lys Ala Ala Ala Ile Ala
    930                 935
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Met Ala Leu Ile Asp Leu Glu Asp Lys Ile Ala Glu Ile Val Asn Arg
1               5                   10                  15
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Glu Asp His Ser Asp Phe Leu Tyr Glu Leu Leu Gly Val Tyr Asp Val
            20                  25                  30

Pro Arg Ala Thr Ile Thr Arg Leu Lys Lys Gly Asn Gln Asn Leu Thr
        35                  40                  45

Lys Arg Val Gly Glu Val His Leu Lys Asn Lys Val Trp Phe Lys Glu
    50                  55                  60

Ala Lys Lys Gly Lys Leu Phe Asp Ala Leu Ile Asp Ile Glu Gln Gln
65                  70                  75                  80

Val Glu Tyr Leu Ser Ala Lys Pro Arg Tyr Leu Leu Val Thr Asp Tyr
                85                  90                  95

Asp Gly Val Leu Ala Lys Asp Thr Lys Thr Leu Glu Ala Leu Asp Val
            100                 105                 110

Lys Phe Glu Glu Leu Pro Gln Tyr Phe Asp Phe Phe Leu Ala Trp Lys
        115                 120                 125

Gly Ile Glu Lys Val Glu Phe Glu Lys Glu Asn Pro Ala Asp Ile Lys
    130                 135                 140

Ala Ala Glu Arg Phe Ala Arg Ile Tyr Asp Val Leu Arg Lys Glu Asn
145                 150                 155                 160

Asn Ile Ile Glu Thr Asn Arg Gly Leu Asp Leu Phe Leu Ile Arg Leu
                165                 170                 175

Leu Phe Cys Phe Phe Ala Glu Asp Thr Asp Ile Phe Lys Arg Asn Ser
            180                 185                 190

Phe Thr Asn Leu Ile Lys Thr Leu Thr Glu Glu Asp Gly Ser Asn Leu
        195                 200                 205

Asn Lys Leu Phe Ala Asp Leu Phe Ile Val Leu Asp Lys Asn Glu Arg
    210                 215                 220

Asp Asp Val Pro Ser Tyr Leu Lys Glu Phe Pro Tyr Val Asn Gly Gln
225                 230                 235                 240

Leu Phe Thr Glu Pro His Thr Glu Leu Glu Phe Ser Ala Lys Ser Arg
                245                 250                 255

Lys Leu Ile Ile Glu Cys Gly Glu Leu Leu Asn Trp Ala Lys Ile Asn
            260                 265                 270
```

```
Pro Asp Ile Phe Gly Ser Met Ile Gln Ala Val Ala Ser Glu Glu Ser
        275                 280                 285

Arg Ser Tyr Leu Gly Met His Tyr Thr Ser Val Pro Asn Ile Met Lys
    290                 295                 300

Val Ile Lys Pro Leu Phe Leu Asp Lys Leu Asn Gln Ser Phe Leu Asp
305                 310                 315                 320

Ala Tyr Asp Asp Tyr Thr Lys Leu Glu Asn Leu Leu Thr Arg Ile Gly
                325                 330                 335

Lys Ile Lys Phe Phe Asp Pro Ala Cys Gly Ser Gly Asn Phe Leu Ile
            340                 345                 350

Ile Thr Tyr Lys Glu Leu Arg Arg Met Glu Ile Asn Ile Ile Lys Arg
        355                 360                 365

Leu Gln Glu Leu Leu Gly Glu Tyr Leu Tyr Val Pro Ser Val Thr Leu
    370                 375                 380

Ser Gln Phe Tyr Gly Ile Glu Ile Glu Asp Phe Ala His Asp Val Ala
385                 390                 395                 400

Lys Leu Ser Leu Trp Ile Ala Glu His Gln Met Asn Glu Glu Leu Lys
                405                 410                 415

Asn Glu Val His Asn Ala Val Arg Pro Thr Leu Pro Leu His Thr Ala
            420                 425                 430

Gly Asp Ile Arg Cys Ala Asn Ala Ile Arg Val Glu Trp Thr Glu Val
        435                 440                 445

Cys Pro Ala Gln Gly Ser Glu Glu Val Tyr Val Phe Gly Asn Pro Pro
    450                 455                 460

Tyr Leu Gly Ser Lys Lys Gln Asn Lys Glu His Lys Ser Asp Met Leu
465                 470                 475                 480

Ser Ile Phe Gly Lys Val Lys Asn Gly Lys Met Leu Asp Tyr Ile Ser
                485                 490                 495

Ala Trp Phe Tyr Phe Gly Ala Lys Tyr Ala Ser Thr Thr Asn Ala Lys
            500                 505                 510

Val Ala Phe Val Ser Thr Asn Ser Val Thr Gln Gly Glu Gln Val Ser
        515                 520                 525
```

```
Ile Leu Trp Asn Glu Leu Phe Lys Phe Gly Ile Gln Ile Asn Phe Ala
    530                 535                 540

Tyr Lys Ser Phe Lys Trp Ala Asn Asn Ala Lys Asn Asn Ala Ala Val
545                 550                 555                 560

Ile Val Val Ile Val Gly Phe Gly Pro Leu Asp Thr Lys Val Asn Lys
                565                 570                 575

Tyr Leu Phe Val Asp Glu Thr Lys Lys Leu Val Ser Asn Ile Ser Pro
            580                 585                 590

Tyr Leu Thr Asp Gly Glu Asn Ile Leu Val Ser Ser Arg Thr Lys Pro
        595                 600                 605

Ile Ser Asp Leu Pro Lys Leu His Phe Gly Asn Met Pro Asn Asp Gly
    610                 615                 620

Gly Gly Leu Leu Phe Thr Ile Thr Glu Tyr Thr Asp Ala Ile Asn Lys
625                 630                 635                 640

Tyr Pro Glu Leu Val Pro Tyr Phe Lys Lys Phe Ile Gly Ser Val Glu
                645                 650                 655

Phe Ile Asn Gly Gly Leu Arg Tyr Cys Leu Trp Leu Asn Glu Ala Lys
            660                 665                 670

Tyr Glu Lys Ile Lys Ser Asn Pro Leu Ile Gln Glu Arg Ile Ser Ile
        675                 680                 685

Ser Lys Asn His Arg Glu Lys Ser Thr Asp Lys Gly Thr Asn Lys Leu
    690                 695                 700

Ala Leu Thr Pro Trp Lys Phe Arg Asp Thr His Glu Thr Thr Asn Tyr
705                 710                 715                 720

Ser Ile Val Val Pro Ser Val Ser Ser Glu Asn Arg Phe Tyr Ile Pro
                725                 730                 735

Met Gly Leu Ala Gly Ala Asp Thr Ile Leu Ser Asn Leu Ile Tyr Val
            740                 745                 750

Ile Tyr Asp Ala Glu Ile Tyr Leu Leu Gly Ile Leu Met Ser Arg Met
        755                 760                 765

His Met Thr Trp Val Lys Ala Val Ala Gly Arg Leu Lys Thr Asp Tyr
```

770 775 780

Arg Tyr Ser Ala Gly Leu Cys Tyr Asn Thr Phe Pro Ile Pro Glu Leu
785 790 795 800

Ser Thr Arg Arg Lys Asn Glu Ile Glu Glu Ala Ile Leu Glu Ile Leu
805 810 815

Asp Leu Arg Glu Glu Gln Gly Gly Thr Leu Ala Glu Leu Tyr Asn Pro
820 825 830

Ser Thr Met Pro Ile Glu Leu Lys Val Ala His Glu Lys Leu Asp Gly
835 840 845

Ile Val Glu Arg Ala Tyr Arg Gln Lys Gln Phe Glu Ser Asp Glu Glu
850 855 860

Arg Leu Glu Val Leu Leu Lys Leu Tyr Gln Glu Met Thr Glu Arg
865 870 875

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<213> unknown

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Met Val Met Ala Pro Thr Thr Val Phe Asp Arg Ala Thr Ile Arg His
1 5 10 15

Asn Leu Thr Glu Phe Lys Leu Arg Trp Leu Asp Arg Ile Lys Gln Trp
20 25 30

Glu Ala Glu Asn Arg Pro Ala Thr Glu Ser Ser His Asp Gln Gln Phe
35 40 45

Trp Gly Asp Leu Leu Asp Cys Phe Gly Val Asn Ala Arg Asp Leu Tyr
50 55 60

Leu Tyr Gln Arg Ser Ala Lys Arg Ala Ser Thr Gly Arg Thr Gly Lys
65 70 75 80

Ile Asp Met Phe Met Pro Gly Lys Val Ile Gly Glu Ala Lys Ser Leu
85 90 95

Gly Val Pro Leu Asp Asp Ala Tyr Ala Gln Ala Leu Asp Tyr Leu Leu
100 105 110

```
Gly Gly Thr Ile Ala Asn Ser His Met Pro Ala Tyr Val Val Cys Ser
        115                 120                 125

Asn Phe Glu Thr Leu Arg Val Thr Arg Leu Asn Arg Thr Tyr Val Gly
    130                 135                 140

Asp Ser Ala Asp Trp Asp Ile Thr Phe Pro Leu Ala Glu Ile Asp Glu
145                 150                 155                 160

His Ile Glu Gln Leu Ala Phe Leu Ala Asp Tyr Glu Thr Ser Ala Tyr
                165                 170                 175

Arg Glu Glu Glu Lys Ala Ser Leu Glu Ala Ser Arg Leu Met Val Glu
            180                 185                 190

Leu Phe Arg Ala Met Asn Gly Asp Asp Val Asp Glu Ala Val Gly Asp
        195                 200                 205

Asp Ala Pro Thr Thr Pro Glu Glu Glu Asp Glu Arg Val Met Arg Thr
    210                 215                 220

Ser Ile Tyr Leu Thr Arg Ile Leu Phe Leu Leu Phe Gly Asp Asp Ala
225                 230                 235                 240

Gly Leu Trp Asp Thr Pro His Leu Phe Ala Asp Phe Val Arg Asn Glu
                245                 250                 255

Thr Thr Pro Glu Ser Leu Gly Pro Gln Leu Asn Glu Leu Phe Ser Val
            260                 265                 270

Leu Asn Thr Ala Pro Glu Lys Arg Pro Lys Arg Leu Pro Ser Thr Leu
        275                 280                 285

Ala Lys Phe Pro Tyr Val Asn Gly Ala Leu Phe Ala Glu Pro Leu Ala
    290                 295                 300

Ser Glu Tyr Phe Asp Tyr Gln Met Arg Glu Ala Leu Leu Ala Ala Cys
305                 310                 315                 320

Asp Phe Asp Trp Ser Thr Ile Asp Val Ser Val Phe Gly Ser Leu Phe
                325                 330                 335

Gln Leu Val Lys Ser Lys Glu Ala Arg Arg Ser Asp Gly Glu His Tyr
            340                 345                 350

Thr Ser Lys Ala Asn Ile Met Lys Thr Ile Gly Pro Leu Phe Leu Asp
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355 360 365

Glu Leu Arg Ala Glu Ala Asp Lys Leu Val Ser Ser Pro Ser Thr Ser
370 375 380

Val Ala Ala Leu Glu Arg Phe Arg Asp Ser Leu Ser Glu Leu Val Phe
385 390 395 400

Ala Asp Met Ala Cys Gly Ser Gly Asn Phe Leu Leu Leu Ala Tyr Arg
405 410 415

Glu Leu Arg Arg Ile Glu Thr Asp Ile Ile Val Ala Ile Arg Gln Arg
420 425 430

Arg Gly Glu Thr Gly Met Ser Leu Asn Ile Glu Trp Glu Gln Lys Leu
435 440 445

Ser Ile Gly Gln Phe Tyr Gly Ile Glu Leu Asn Trp Trp Pro Ala Lys
450 455 460

Ile Ala Glu Thr Ala Met Phe Leu Val Asp His Gln Ala Asn Lys Glu
465 470 475 480

Leu Ala Asn Ala Val Gly Arg Pro Pro Glu Arg Leu Pro Ile Lys Ile
485 490 495

Thr Ala His Ile Val His Gly Asn Ala Leu Gln Leu Asp Trp Ala Asp
500 505 510

Ile Leu Ser Ala Ser Ala Ala Lys Thr Tyr Ile Phe Gly Asn Pro Pro
515 520 525

Phe Leu Gly His Ala Thr Arg Thr Ala Glu Gln Ala Gln Glu Leu Arg
530 535 540

Asp Leu Trp Gly Thr Lys Asp Ile Ser Arg Leu Asp Tyr Val Thr Gly
545 550 555 560

Trp His Ala Lys Cys Leu Asp Phe Phe Lys Ser Arg Glu Gly Arg Phe
565 570 575

Ala Phe Val Thr Thr Asn Ser Ile Thr Gln Gly Asp Gln Val Pro Arg
580 585 590

Leu Phe Gly Pro Ile Phe Lys Ala Gly Trp Arg Ile Arg Phe Ala His
595 600 605

```
Arg Thr Phe Ala Trp Asp Ser Glu Ala Pro Gly Lys Ala Ala Val His
    610                 615                 620

Cys Val Ile Val Gly Phe Asp Lys Glu Ser Gln Pro Arg Pro Arg Leu
625                 630                 635                 640

Trp Asp Tyr Pro Asp Val Lys Gly Glu Pro Val Ser Val Glu Val Gly
                645                 650                 655

Gln Ser Ile Asn Ala Tyr Leu Val Asp Gly Pro Asn Val Leu Val Asp
            660                 665                 670

Lys Ser Arg His Pro Ile Ser Ser Glu Ile Ser Pro Ala Thr Phe Gly
        675                 680                 685

Asn Met Ala Arg Asp Gly Gly Asn Leu Leu Val Glu Val Asp Glu Tyr
    690                 695                 700

Asp Glu Val Met Ser Asp Pro Val Ala Ala Lys Tyr Val Arg Pro Phe
705                 710                 715                 720

Arg Gly Ser Arg Glu Leu Met Asn Gly Leu Asp Arg Trp Cys Leu Trp
                725                 730                 735

Leu Val Asp Val Ala Pro Ser Asp Ile Ala Gln Ser Pro Val Leu Lys
            740                 745                 750

Lys Arg Leu Glu Ala Val Lys Ser Phe Arg Ala Asp Ser Lys Ala Ala
        755                 760                 765

Ser Thr Arg Lys Met Ala Glu Thr Pro His Leu Phe Gly Gln Arg Ser
    770                 775                 780

Gln Pro Asp Thr Asp Tyr Leu Cys Leu Pro Lys Val Val Ser Glu Arg
785                 790                 795                 800

Arg Ser Tyr Phe Thr Val Gln Arg Tyr Pro Ser Asn Val Ile Ala Ser
                805                 810                 815

Asp Leu Val Phe His Ala Gln Asp Pro Asp Gly Leu Met Phe Ala Leu
            820                 825                 830

Ala Ser Ser Ser Met Phe Ile Thr Trp Gln Lys Ser Ile Gly Gly Arg
        835                 840                 845

Leu Lys Ser Asp Leu Arg Phe Ala Asn Thr Leu Thr Trp Asn Thr Phe
    850                 855                 860
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Pro Val Pro Glu Leu Asp Glu Lys Thr Arg Gln Arg Ile Ile Lys Ala
865 870 875 880

Gly Lys Lys Val Leu Asp Ala Arg Ala Leu His Pro Glu Arg Ser Leu
885 890 895

Ala Glu His Tyr Asn Pro Leu Ala Met Ala Pro Glu Leu Ile Lys Ala
900 905 910

His Asp Ala Leu Asp Arg Glu Val Asp Lys Ala Phe Gly Ala Pro Arg
915 920 925

Lys Leu Thr Thr Val Arg Gln Arg Gln Glu Leu Leu Phe Ala Asn Tyr
930 935 940

Glu Lys Leu Ile Ser His Gln Pro
945 950

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Pro Ala Asp Glu Arg Ser Gln Met Asp Ala Gly Gly Lys Pro Val Glu
1 5 10 15

Gly Gly Asn Leu Leu Phe Ala Glu Glu Glu Lys Gln Arg Leu Val Glu
20 25 30

Gly Asn Val Asp Val Val Lys Phe Leu Lys Arg Val Tyr Gly Ala Ser
35 40 45

Glu Tyr Ile Arg Gly Glu Val Arg Phe Cys Leu Trp Ile Ser Asp Ser
50 55 60

Gln Glu Gln Glu Ala Lys Ser Asn Ser Asp Ile Asn Cys Lys Leu Asn
65 70 75 80

Ala Val Ala Ala Phe Arg Leu Lys Ser Pro Lys Ala Ala Thr Lys Lys
85 90 95

Gly Ala Ala Trp Pro His Lys Phe Glu Glu Val Lys Gln Ile Gly Asn
100 105 110

Glu Val Val Thr Ile Val Pro Lys Val Ser Ser Glu Ser Arg Glu Tyr
115 120 125

Leu Pro Val Gly Leu Leu Pro Arg Gly Ser Ile Val Thr Asp Leu Ala
130 135 140

Phe Ala Leu Tyr Asp Ala Pro Leu Trp Asn Met Ala Leu Ile Ala Ser
145 150 155 160

Arg Leu His Leu Val Trp Ile Gly
165

<210> 10
<211> 909
<212> PRT
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<400> 10

Met Asn Pro Val Glu Ile Glu Glu Ala Val Ser Asp Leu Ala Arg Ala
1 5 10 15

Pro Tyr Asp Ala Ser Glu Phe Pro Phe Gln Phe Leu Ala Ala Phe Gly
20 25 30

Asn Lys Gln Thr Thr Leu Gln Arg Leu Arg Ala Gly Asn Ser Asn Gln
35 40 45

Ser Asp Leu Pro Gly Ala Val Leu Gln Arg Asn His Ile His Ile Ala
50 55 60

Thr Cys Asp Ala Gly Asn Val Asp Arg Thr Leu Ala Ala Leu Arg Lys
65 70 75 80

Ser Pro Lys Thr Ala Ser Gln Lys Ala Arg Phe Ile Leu Ala Thr Asp
85 90 95

Gly Val Ala Phe Gln Ala Glu Asp Met Ala Ser Gly Glu Thr Val Ala
100 105 110

Cys Asn Tyr Ala Ala Phe Pro Asp Lys Phe Ala Phe Phe Leu Pro Leu
115 120 125

Ala Gly Ile Thr Thr Val Gln Gln Ile Arg Glu Ser Ser Phe Asp Ile
130 135 140

Lys Ala Thr Gly Arg Leu Asn Lys Leu Tyr Val Glu Leu Leu Lys Asp

```
145                 150                 155                 160

Asn Pro Asp Trp Ala Ser Arg Ser Glu Asp Met Asn His Phe Met Ala
                165                 170                 175

Arg Leu Ile Phe Cys Phe Phe Ala Glu Asp Thr Asp Ile Phe Val Gly
            180                 185                 190

Glu Gly Leu Phe Ser Arg Thr Val Glu Thr Met Ser Ala Arg Asp Ala
        195                 200                 205

Ser Asp Thr His Met Val Ile Ala Glu Ile Phe Arg Ala Met Asp Thr
    210                 215                 220

Arg Leu Ala Asp Arg Ala Ala Ala Gly Ile Lys Ser Trp Ala Asp Val
225                 230                 235                 240

Phe Pro Tyr Val Asn Gly Gln Leu Phe Ser Gly Ser Thr Glu Cys Pro
                245                 250                 255

Arg Phe Ser Lys Ile Ala Arg Ser Tyr Leu Leu His Ile Gly Ser Leu
            260                 265                 270

Asp Trp Gln Lys Ile Asn Pro Asp Ile Phe Gly Ser Met Ile Gln Ala
        275                 280                 285

Val Ala Asp Asp Glu Glu Arg Gly Ala Leu Gly Met His Tyr Thr Ser
    290                 295                 300

Val Pro Asn Ile Leu Lys Val Leu Asn Pro Leu Phe Leu Asp Asp Leu
305                 310                 315                 320

Arg Ala Lys Leu Glu Glu Ala Gly Asp Asn Ser Arg Lys Leu Leu Asn
                325                 330                 335

Leu Arg Asn Arg Met Ala Lys Ile Arg Val Phe Asp Pro Ala Cys Gly
            340                 345                 350

Ser Gly Asn Phe Leu Val Ile Ala Tyr Lys Gln Met Arg Glu Leu Glu
        355                 360                 365

Ala Glu Ile Asn Arg Arg Arg Gly Glu Ala Asp Arg Arg Ser Asp Ile
    370                 375                 380

Pro Leu Thr Asn Phe Arg Gly Ile Glu Leu Arg Asn Phe Pro Ala Glu
385                 390                 395                 400
```

```
Ile Ala Arg Leu Ala Leu Ile Ile Ala Glu Tyr Gln Cys Asp Val Leu
                405                 410                 415

Tyr Arg Gly Gln Lys Glu Ala Leu Ala Glu Phe Leu Pro Leu Asp Ser
            420                 425                 430

Gln Asn Trp Ile Thr Cys Gly Asn Ala Leu Arg Leu Asp Trp Leu Ser
        435                 440                 445

Ile Cys Pro Pro Thr Gly Thr Ala Val Lys Leu Gln Ala Asn Asp Leu
    450                 455                 460

Phe Glu Met Pro Leu Asp Gln Ala Glu Ile Asp Phe Glu Asn Glu Gly
465                 470                 475                 480

Gly Glu Thr Tyr Ile Cys Gly Asn Pro Pro Tyr Leu Gly Ala Lys Lys
                485                 490                 495

Lys Ser Ser Asp Gln Ile Glu Asp Met Lys Arg Val Gly Leu Asp Lys
            500                 505                 510

Ala Gln Leu Leu Asp Tyr Val Ser Ala Phe Ile Val Arg Gly Leu Pro
        515                 520                 525

Leu Val Ala Gln Gln Arg Cys Asp Met Ala Leu Val Ser Thr Ser Ser
    530                 535                 540

Ile Cys Gln Gly Glu Gln Val Ser Leu Ile Trp Pro Arg Ile Leu Lys
545                 550                 555                 560

Ser Ala Asn Val Lys Phe Ala Tyr Arg Pro Phe Arg Trp Ser Asn Ser
                565                 570                 575

Ala Ala Asn Asn Ala Gly Val Tyr Cys Thr Ile Ile Gly Leu Thr Gly
            580                 585                 590

Ser Glu Val Ser Asn Lys Lys Leu Phe Gly Glu Gly Ser Val Val Glu
        595                 600                 605

Cys Ser Ser Ile Ala Pro Tyr Leu Val Pro Gly Pro Glu Ile Ile Cys
    610                 615                 620

Ala Pro Arg Gln Ser Ser Ile Ser Gly Phe Ala Arg Met Val Met Gly
625                 630                 635                 640

Ser Asn Pro Val Asp Gly Lys Arg Leu Ile Phe Glu Gln Asp Glu Lys
                645                 650                 655
```

```
Glu Ser Val Val Ala Ala Asp Pro Arg Ser Glu Arg Phe Phe Lys Arg
            660                 665                 670

Tyr Gly Gly Thr Gln Glu Leu Val Asn Gly Val Asp Arg Trp Cys Leu
        675                 680                 685

Trp Ile Asn Asp Asp Gln Val Asp Asp Ala Lys Ala Ile Ala Glu Ile
    690                 695                 700

Ala Lys Val Leu Glu Ser Cys Arg Ser Tyr Arg Gln Gly Ala Gly Arg
705                 710                 715                 720

Asp Ala Gln Lys Ala Ala Asn Arg Pro His Ser Phe Cys Tyr Arg Thr
                725                 730                 735

Phe Gln Glu Asn Ile Gly Ile His Val Gly Leu Thr Ile Gly Asn Gly
            740                 745                 750

Leu Ser His Val Pro Ala Asp Leu Lys Ser Ser Gly Phe Val Ser Ser
        755                 760                 765

His Thr Ala Tyr Met Ile Tyr Gly Trp His Pro Val Glu Phe Ala Leu
    770                 775                 780

Leu Asn Ser Arg Leu Met Leu Val Trp Thr Glu Thr Val Gly Gly Arg
785                 790                 795                 800

Leu Gly Asn Gly Met Arg Phe Ser Asn Thr Ile Val Tyr Asn Thr Phe
                805                 810                 815

Pro Val Pro Ser Leu Thr Asp Gln Asn Lys Ala Asp Leu Thr Arg Cys
            820                 825                 830

Ala Glu Asp Ile Leu Leu Ala Arg Glu Ser His Phe Pro Ala Thr Ile
        835                 840                 845

Ala Asp Leu Tyr Asp Pro Glu Thr Met Pro Glu Ser Leu Arg Ala Ala
    850                 855                 860

His Asp Arg Asn Asp Glu Val Leu Glu Arg Ile Tyr Ile Gly Arg Arg
865                 870                 875                 880

Phe Arg Asn Asp Thr Glu Arg Leu Glu Lys Leu Phe Glu Leu Tyr Thr
                885                 890                 895

Lys Met Thr Gly Gly Arg Ser Ser Glu Gly Gly Ala Ala
            900                 905
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1               5                   10                  15

Ile Lys Lys Trp Arg Lys Ser Glu Leu Gly Glu Arg Gln Ala Ala Gln
            20                  25                  30

Glu His Phe Leu Asp Ile Cys Ser Leu Val Gly His Pro Ser Pro Ser
        35                  40                  45

Asp Glu Asp Pro Thr Gly Ala Phe Phe Ala Phe Glu Lys Gly Ala Asn
    50                  55                  60

Lys Leu Gly Gly Gly Lys Gly Phe Ala Asp Val Trp Lys Lys Gly His
65                  70                  75                  80

Phe Ala Trp Glu Tyr Lys Arg Lys Lys Gly Asn Leu Asp Glu Ala Leu
                85                  90                  95

Leu Gln Leu Met Arg Tyr Ala Pro Ala Leu Leu Ser Pro Pro Leu His
            100                 105                 110

Ile Val Cys Asp Ile Glu Arg Leu Arg Ile His Thr Ala Trp Thr Asn
        115                 120                 125

Thr Val Pro Ser Thr Tyr Val Ile Thr Leu Asp Asp Leu Ala Glu Pro
    130                 135                 140

Ser Ala Arg Glu Met Leu His Asn Val Phe Phe Ser Pro Glu Lys Leu
145                 150                 155                 160

Arg Pro Thr Arg Thr Arg Ala Ala Val Thr Lys Glu Ala Ala Asp Lys
                165                 170                 175

Phe Ser Ala Ile Ala Leu Arg Val Gln Gly Arg Gly Thr Pro Asp Glu
            180                 185                 190

Ile Ala His Phe Val Asn Gln Leu Val Phe Cys Phe Phe Ala Gln Ser
        195                 200                 205
```

```
Val Ser Leu Leu Pro Asp Gly Leu Phe Thr Lys Leu Leu Lys Arg Ser
    210                 215                 220

Ala Arg Ala Pro Glu Arg Ala Met Ser Tyr Leu Asp Lys Leu Phe Glu
225                 230                 235                 240

Ala Met Glu Arg Gly Gly Glu Phe Asp Leu Thr Asp Ile Thr Trp Phe
                245                 250                 255

Asn Gly Gly Leu Phe Asp Gly Arg Arg Ala Leu Arg Leu Asp Asp Gly
            260                 265                 270

Asp Ile Gly Leu Leu Val Ala Ala Asp Ser Leu Asp Trp Gly Leu Ile
        275                 280                 285

Asp Pro Thr Ile Phe Gly Thr Leu Phe Glu Arg Phe Leu Asp Pro Glu
    290                 295                 300

Lys Arg Ala Gln Ile Gly Ala His Tyr Thr Asp Pro Glu Lys Ile Met
305                 310                 315                 320

Arg Leu Val Asp Pro Val Ile Leu Arg Pro Leu Arg Gln Glu Trp Glu
                325                 330                 335

Gln Ala Arg Arg Glu Ile Val Glu Leu Leu Asn Gly Asn Arg Lys Pro
            340                 345                 350

Pro Met Arg Arg Gln Gln Ser Arg Arg Met Lys Arg Glu Glu Ala Ala
        355                 360                 365

Ala Glu Val Arg Ser Arg Phe Thr Glu Arg Leu Arg Lys Leu Arg Ile
    370                 375                 380

Leu Asp Pro Ala Cys Gly Ser Gly Asn Phe Leu Tyr Leu Ala Leu Gln
385                 390                 395                 400

Gly Val Lys Asp Ile Glu His Arg Ala Asn Leu Asp Cys Glu Met Leu
                405                 410                 415

Gly Met Pro Ala Gln Leu Pro Leu Val Gly Pro Glu Ile Leu Arg Gly
            420                 425                 430

Ile Glu Ile Asn Met Met Ala Ala Glu Leu Ala Arg Thr Thr Ile Trp
        435                 440                 445

Ile Gly Asp Ile Gln Trp Gln Ile Lys Asn Gly Ile Arg Ser Lys Ser
    450                 455                 460
```

```
Ile Pro Ile Leu Arg Lys Leu Asp Ala Ile Glu Arg Arg Asp Ala Leu
465                 470                 475                 480

Val Arg Gln Ala Gln Asp Val Asp Thr Ala Arg Asp Ala Gln Gly Asp
                485                 490                 495

Leu Leu Ala Ala Leu Gln Pro Val Ser Glu Asp Ala Glu Ala Glu Trp
            500                 505                 510

Pro Glu Ala Glu Phe Ile Val Gly Asn Pro Pro Phe Val Gly Val Arg
        515                 520                 525

Leu Met Arg Gln Ala Leu Gly Asp Pro Thr Val Asp Arg Leu Phe Asp
    530                 535                 540

Val Tyr Asp Gly Arg Val Ser Arg Glu Ala Asp Leu Val Cys Tyr Trp
545                 550                 555                 560

Val Glu Lys Ser Arg Ala Ala Val Ala Ala Asp Arg Thr Arg Arg Val
                565                 570                 575

Gly Leu Val Thr Thr Asn Ser Ile Arg Gly Gly Ala Asn Arg Arg Val
            580                 585                 590

Leu Asp Arg Ile Ile Ala Glu Ser Arg Leu Phe Glu Ala Trp Ser Asp
        595                 600                 605

Glu Pro Trp Val Val Asp Gly Ala Ala Val Arg Val Ser Leu Ile Cys
    610                 615                 620

Phe Gly His Gly Glu Asp Pro Leu Cys Leu Asp Gly Arg Thr Val Ala
625                 630                 635                 640

Gln Ile Asn Ala Asp Leu Thr Ala Gly Val Thr Asp Leu Thr Lys Ala
                645                 650                 655

Arg Arg Leu Ser Glu Asn Gln Asn Val Ala Phe Met Gly Asp Thr Lys
            660                 665                 670

Gly Gly Ala Phe Asp Val Pro Gly Ser Leu Ala Arg Ala Trp Leu Ser
        675                 680                 685

Met Pro Met Asn Pro Asn Gly Arg Pro Asn Ser Asp Val Leu Arg Pro
    690                 695                 700

Trp Arg Asn Gly Met Asp Val Ala Arg Arg Gly Arg Asp Met Trp Ile
```

```
705                 710                 715                 720

Val Asp Phe Gly Trp Glu Met Ser Glu Gln Glu Ala Ala Leu Tyr Glu
                725                 730                 735

Ala Pro Phe Gln His Ile Arg Glu His Val Phe Pro Glu Arg Ser Lys
            740                 745                 750

Asn Arg Arg Asp Ala Tyr Arg Glu Arg Trp Trp Arg His Val Glu Pro
        755                 760                 765

Arg Pro Ala Phe His Ala Ser Leu Gln Gly His Ser Arg Tyr Met Ala
    770                 775                 780

Thr Pro Arg Val Ala Lys His Arg Thr Phe Val Trp Leu Asp Gln Ala
785                 790                 795                 800

Ile Val Pro Asp Ser Arg Ile Phe Ala Phe Ser Arg Ser Asp Asp Val
                805                 810                 815

Phe Phe Gly Ile Leu His Ser Arg Phe His Glu Ala Trp Ser Phe Gly
            820                 825                 830

Thr Cys Ser Trp His Gly Val Gly Asn Asp Pro Thr Tyr Asn Ser Ala
        835                 840                 845

Gly Val Phe Glu Thr Phe Pro Phe Pro Glu Gly Leu Thr Pro Asp Ile
    850                 855                 860

Pro Ala Val Arg Tyr Glu Lys Asp Ser Arg Ala Ile Ala Ile Ser Lys
865                 870                 875                 880

Ala Ala Lys Arg Leu Asp Asp Ile Arg Asn Ala Trp Leu Asn Pro Ser
                885                 890                 895

Asp Leu Val Gln Ile Lys Pro Glu Val Val Pro Gly Tyr Pro Asp Arg
            900                 905                 910

Ile Leu Pro Lys Asp Ile Ala Ser Asp Ala Ile Leu Arg Asp Arg Thr
        915                 920                 925

Leu Thr Asn Leu Tyr Asn Arg Arg Pro Gln Trp Leu Val Asp Ala His
    930                 935                 940

Ser Asp Leu Asp Ala Ala Val Ala Gly Ala Tyr Gly Trp Pro Ala Asp
945                 950                 955                 960
```

```
Ile Ser Glu Asp Glu Ala Leu Ala Asn Leu Leu Glu Leu Asn Leu Ala
                965                 970                 975

Arg Glu Ala Phe Asn Glu His Ala Lys Ser Gly Leu Lys Thr Arg Lys
            980                 985                 990

Pro Arg Arg Arg Pro Thr Pro Glu  Glu Val Arg Arg Ala  Pro Gln Met
        995                 1000                1005

Lys Leu  Pro Ile Ala Gly Gly  Arg Lys Ser Val Val  Gly Pro Gln
    1010                1015                1020

Gln Leu  Thr Thr Lys Asp Arg  Glu Asn Gln Pro Thr  Ser Ala Glu
    1025                1030                1035

Arg Pro  Arg Asn Thr Lys Arg  Arg Thr Ser
    1040                1045
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1               5                   10                  15

Leu Gly Glu Arg Tyr Cys Phe Glu Arg Gly Ala Ala Lys Thr Gly Gly
            20                  25                  30

Gly Asp Gly Trp Ala Asp Val Trp Arg Lys Gly Cys Phe Gly Trp Glu
        35                  40                  45

Tyr Lys Gly Lys His Lys Asn Leu Asp Ala Ala Leu Arg Gln Leu Gln
    50                  55                  60

Ala Tyr Ala Leu Asp Leu Gln Asn Pro Pro Tyr Leu Val Val Ser Asp
65                  70                  75                  80

Met Glu Arg Ile Ile Val His Thr Asn Trp Thr Asn Thr Ile Ser Arg
                85                  90                  95

Lys Ile Glu Phe Thr Leu Asp Asp Leu His Glu Pro Glu Lys Leu Ala
            100                 105                 110

Met Leu Arg Gln Val Phe Asp Gly Ser Asp Ser Leu Lys Pro Lys Ile
```

115 120 125

Ser Pro Gln Glu Leu Thr Ala Lys Val Ala Gln Arg Phe Gly Asp Leu
130 135 140

Gly Arg Arg Leu Gln Glu Arg Gly His His Pro Arg Asp Val Ala His
145 150 155 160

Phe Leu Asn Arg Val Val Phe Cys Met Phe Ala Glu Asp Ala Lys Leu
165 170 175

Leu Pro Glu Gly Leu Phe Thr Arg Leu Thr Arg Ser Met Gln Met Arg
180 185 190

Pro Pro Ala Glu Ala Ala Pro Gln Phe Asp Ala Leu Phe Ala Met Met
195 200 205

Arg Ala Gly Gly Met Phe Gly Ala Asp Ile Val His Trp Phe Asn Gly
210 215 220

Gly Leu Phe Asp Glu Lys Pro Ala Leu Pro Leu Glu Arg Ala Asp Ile
225 230 235 240

Lys Leu Ile His Asp Thr Ala Ala Glu His Asp Trp Ser Asp Leu Asp
245 250 255

Pro Ser Val Phe Gly Asn Met Phe Glu Glu Ala Leu Lys Ala Thr Arg
260 265 270

Glu Arg Ala Ala Leu Gly Ala His Tyr Thr Asp Arg Glu Lys Ile Leu
275 280 285

Lys Ile Ile Asp Pro Val Ile Thr Trp Pro Leu Met Ala Gln Trp Glu
290 295 300

Thr Ala Leu Ala Glu Ile Arg Ala Ala Leu Asp Ala Arg Ala Ala Ala
305 310 315 320

Glu Ala Glu Arg Lys Ala Val Leu Glu Ala Ala Ala Glu Ala Met Arg
325 330 335

Ala Asp Pro Val Lys Ala Lys Ala Gly Glu Ala Ala Arg Arg Lys Thr
340 345 350

Leu Thr Ala Ile Ala Lys Arg Ser Asp Ala Ala Leu Gly Gln Ala Lys
355 360 365

```
Asp Arg Leu Glu Ala Phe Leu Ser Arg Leu Ala Ala Phe Arg Val Leu
    370                 375                 380

Asp Pro Ala Cys Gly Ser Gly Asn Phe Leu Tyr Val Ala Leu His Ala
385                 390                 395                 400

Leu Lys Asp Ile Glu Arg Arg Ala Leu Val Asp Ala Glu Arg Leu Gly
                405                 410                 415

Leu Glu Val Pro Thr Pro Arg Val Gly Leu Ala Cys Val Arg Gly Ile
            420                 425                 430

Glu Ile Glu Glu Tyr Ala Ala Glu Leu Ala Arg Val Thr Leu Trp Ile
        435                 440                 445

Gly Asp Leu Gln Trp His Ala Lys Asn Asn Tyr Arg Gly Phe Ala Glu
    450                 455                 460

Pro Ile Leu Ser Ser Leu Asp Gln Ile Glu Cys Arg Asp Ala Leu Leu
465                 470                 475                 480

Asn Ala Asp Gly Thr Glu Ala Gln Trp Pro Ala Val Asp Val Ile Val
                485                 490                 495

Gly Asn Pro Pro Phe Leu Gly Ser Lys Arg Leu Arg Asp Gly Leu Gly
            500                 505                 510

Asn Asp Tyr Val Glu Arg Leu Phe Ser Thr Tyr Arg Gly Lys Val Pro
        515                 520                 525

Ala Glu Ala Asp Phe Val Ala Tyr Trp Ile Ala Lys Ala Trp Glu Leu
    530                 535                 540

Val Gln Ala Gln Gln Gly Arg Arg Ala Gly Leu Val Thr Thr Asn Ser
545                 550                 555                 560

Val Arg Gly Gly Ala Ser Arg Lys Val Leu Asp Pro Ile Ala Asp Ala
                565                 570                 575

Gly Ala Leu Met Glu Ala Trp Ala Asp Glu Pro Trp Ala Leu Glu Gly
            580                 585                 590

Ala Ala Val Arg Val Ser Met Phe Gly Phe Gly Asp Gly Phe Ala Glu
        595                 600                 605

Arg Arg Leu Glu Gly Arg Lys Ala Glu His Leu His Ser Asp Phe Arg
    610                 615                 620
```

```
Gly Ala Ser Thr Asp Val Thr Lys Ala Leu Arg Leu Lys Glu Asn Ala
625                 630                 635                 640

Ser Ile Ala Phe Met Gly Asp Thr Lys Gly Gly Ala Phe Asp Val Ser
                645                 650                 655

Gly Glu Ile Ala Arg Glu Trp Leu Arg Leu Pro Leu Asn Pro Asn Gly
            660                 665                 670

Arg Pro Asn Ser Asp Val Leu Lys Pro Trp Arg Asn Ala Met Asp Met
        675                 680                 685

Thr Arg Arg Ser Ser Asp Lys Trp Ile Ile Asp Phe Gly Trp Thr Met
    690                 695                 700

Ser Glu Ala Asp Ala Ala Leu Phe Glu Thr Pro Phe Arg His Val Leu
705                 710                 715                 720

Leu His Val Lys Pro Glu Arg Asp Arg Asn Asn Arg Glu Met Tyr Arg
                725                 730                 735

Leu Asn Trp Trp Lys His Val Glu Pro Arg Gln Gly Leu Met Lys Arg
            740                 745                 750

Val Pro Ala Leu Ser Arg Leu Leu Val Thr Pro Glu Val Ser Lys His
        755                 760                 765

Arg Leu Phe Ile Trp Leu Asp Ala Arg Val Leu Pro Asp His Lys Leu
    770                 775                 780

Gln Val Val Thr Leu Asp Asp Asp Cys Ser Phe Gly Val Leu His Ser
785                 790                 795                 800

Arg Phe His Glu Val Trp Ala Leu Ala Ala Gly Ser Trp His Gly Ser
                805                 810                 815

Gly Asn Asp Pro Arg Tyr Thr Ile Ser Thr Thr Phe Glu Thr Phe Pro
            820                 825                 830

Phe Pro Glu Gly Leu Thr Pro Asn Ile Ala Ala Val Asp Tyr Glu Gly
        835                 840                 845

Asp Pro Arg Ala Gln Ala Ile Ala Ala Ala Ala Ala Glu Leu Asn Arg
    850                 855                 860

Leu Arg Glu Ala Trp Leu Asn Pro Pro Asp Leu Val Arg Ile Glu Pro
865                 870                 875                 880
```

Glu Val Val Pro Gly Tyr Pro Asp Arg Val Leu Pro Val Ser Pro Glu
885 890 895

Ala Gly Ala Glu Leu Lys Lys Arg Thr Leu Thr Asn Leu Tyr Asn Gln
900 905 910

Arg Pro Ala Trp Leu Asp Met Ala His Gln Arg Leu Asp Ala Ala Val
915 920 925

Ala Ala Ala Tyr Gly Trp Pro Asp Gly Leu Thr Asp Asp Glu Ile Leu
930 935 940

Glu Arg Leu Phe Ala Leu Asn Gln Glu Arg Ala Ala Ala Gly Arg
945 950 955

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Met His Pro Gln Glu Phe Ala Asp Thr Trp Ser Arg Arg Ala Leu Lys
1 5 10 15

Ala Thr Glu Arg Asp Ser Tyr Val Gln His Trp Leu Asp Leu Cys Gln
20 25 30

Leu Leu His His Glu Ala Pro Gly Ala Asp Pro Asp Tyr Lys Phe Glu
35 40 45

Arg Arg Val Thr Lys Val Gly Thr Lys Asp Lys Gly Phe Ala Asp Val
50 55 60

Phe Lys Lys Ala His Phe Ile Thr Glu Tyr Lys Arg Pro Gly Ser Asp
65 70 75 80

Leu Gly Ala Ala Leu Gln Gln Ala Thr Leu Tyr Ser Arg Asp Leu Gly
85 90 95

Asn Pro Pro Leu Leu Leu Thr Ser Asp Phe Gln Arg Ile Glu Ile Asn
100 105 110

Thr Ala Phe Thr Gly Thr Ser Pro Lys Ser Tyr Leu Ile Thr Leu Asp
115 120 125

```
Asp Ile Ala Glu Asn Arg Val Val Gly Gly Asn Asp Val Pro Ala Leu
    130                 135                 140

Gln Ile Leu His Ser Ala Leu His Gln Pro Tyr Asp Leu Asp Pro Arg
145                 150                 155                 160

Leu Phe Arg Glu Arg Ile Thr Thr Asp Ala Thr Arg Gln Val Gly Leu
                165                 170                 175

Val Ala Arg Arg Leu Gly Glu Arg Glu Gly Arg Thr Arg Ala Ala His
            180                 185                 190

Met Met Met Arg Val Val Phe Ala Leu Phe Ala Glu Asp Thr Gly Met
        195                 200                 205

Leu Glu Arg Gly Ile Val Thr Arg Leu Leu Glu Arg Ala Arg Ala Pro
    210                 215                 220

Pro Gly Glu Asp Gln Leu Tyr Phe Gln Asp Leu Phe Gly Ala Met Lys
225                 230                 235                 240

Gly Gly Gly Glu Phe Trp Gly Thr Asp Ile Arg His Phe Asn Gly Gly
                245                 250                 255

Leu Phe Asp Ser Glu Asp Ala Leu Ala Leu Thr Ser Glu Asp Ala Ala
            260                 265                 270

Ala Leu Ile Ile Ala Ala Lys Leu Asp Trp Ser Glu Val Glu Pro Ser
        275                 280                 285

Ile Phe Gly Thr Leu Phe Glu Asn Ser Leu Asp Val Asp Thr Arg Ser
    290                 295                 300

Arg Arg Gly Ala His Tyr Thr Ser Val Asn Asp Ile Glu Arg Ile Val
305                 310                 315                 320

Asp Arg Val Val Met Glu Pro Leu Trp Ala Glu Trp Asp Ala Leu Arg
                325                 330                 335

Leu Ser Leu Pro Glu Leu Lys Lys Asn Val Arg Leu Glu Arg Leu Phe
            340                 345                 350

Ala Phe Gln Asp Arg Leu Thr Ala Val Arg Ile Leu Asp Pro Ala Cys
        355                 360                 365

Gly Ser Gly Asn Phe Leu Phe Val Ala Leu Lys Lys Leu Leu Asp Leu
    370                 375                 380
```

```
Glu Tyr Gln Val Arg Met Ala Ala Val Met Asn Asp Ile Gly Glu Phe
385                 390                 395                 400

Glu Met Pro Pro Leu Val His Pro Gln Gln Met Leu Gly Ile Glu Ile
                405                 410                 415

Glu Thr Phe Ala His Glu Leu Ala Ser Ile Thr Leu Trp Met Gly Tyr
            420                 425                 430

Phe Gln Trp Lys Arg Ala His Gly Gly His Trp Glu Thr Pro Ile Leu
        435                 440                 445

Gln Arg Leu Asp Asn Ile Gln Asn Arg Asp Ala Leu Leu Asn Pro Asp
    450                 455                 460

Gly Thr Glu Ala Thr Trp Pro Arg Ala Asp Phe Ile Val Gly Asn Pro
465                 470                 475                 480

Pro Phe Leu Gly Asp Lys Met Met Arg Ser Gln Leu Gly Glu Ala Tyr
                485                 490                 495

Thr Thr Gln Leu Arg Glu Thr Phe Lys Asp Arg Leu Pro Gly Gln Ser
            500                 505                 510

Asp Leu Val Cys Tyr Trp Pro Glu Lys Ala Arg Ala Leu Ile Glu Ala
        515                 520                 525

Gly Val Thr Thr Arg Ala Gly Phe Val Thr Thr Asn Ser Ile Arg Gly
    530                 535                 540

Gly Lys Asn Arg Val Val Leu Glu Arg Ile Lys Ala Thr Gly Asp Leu
545                 550                 555                 560

Phe Met Ala Trp Pro Asp Glu Pro Trp Gln Gln Asn Gly Ala Ala Val
                565                 570                 575

Arg Val Ser Leu Phe Gly Phe Asp Asn Gly Thr Glu Thr Leu Arg Thr
            580                 585                 590

Leu Asn Asp Gly His Val Gly Val Ile Asn Ala Asp Leu Asn Ala Gly
        595                 600                 605

Thr Asp Val Lys Gln Ala Gln Lys Leu Pro Glu Asn Ala Gly Val Ser
    610                 615                 620

Phe Ile Gly Thr Gln Lys Gly Gly Ala Phe Asp Ile Pro Gly Asp Leu
```

625 630 635 640

Ala Arg Ser Trp Leu Ser Val Pro Asn Pro Asp Arg Val Ser Asn Ala
645 650 655

Asp Val Leu Lys Pro Trp Val Asn Gly Met Asp Leu Thr Arg Arg Pro
660 665 670

Ser Gly Arg Trp Ile Ile Asp Phe Ala Gln Met Asp Glu Gly Glu Ala
675 680 685

Arg Gln Tyr Leu Gln Pro Met Ala Tyr Val Glu Gln Lys Ile Arg Pro
690 695 700

Glu Arg Ala Thr Asn Ser Asp Arg Pro Ser Arg Glu Arg Trp Trp Leu
705 710 715 720

His Gln Arg Ser Arg Pro Glu Leu Arg Glu Ala Thr Ile Glu Leu Asp
725 730 735

Arg Phe Ile Gly Ile Pro Arg Val Ala Lys His Leu Leu Pro Val Trp
740 745 750

Leu Pro Glu Gly Thr Leu Pro Asp Ser Gln Val Val Val Ile Ala Arg
755 760 765

Asp Asp Asp Phe Ile Phe Gly Val Leu Ala Ser Thr Ile His Arg Ser
770 775 780

Trp Ala Arg Met Gln Gly Thr Tyr Met Gly Val Gly Asn Asp Leu Arg
785 790 795 800

Tyr Thr Pro Ser Thr Cys Phe Glu Thr Phe Pro Val Pro Ala Pro Thr
805 810 815

Asp Glu Gln Arg Ala Glu Ile Glu Lys Trp Ala Lys Tyr Ile Val Gln
820 825 830

Leu Arg Glu His Leu Leu Asn Gln Asp Ala Lys Gly Thr Leu Thr Gly
835 840 845

Ile Tyr Asn Gln Leu Glu Lys Leu Arg Asn Ser Pro Asp Ala Ala His
850 855 860

Pro Val Ser Ala Leu Ala Thr Ala His Asp Lys Leu Asp Gln Ala Val
865 870 875 880

```
Ala Thr Ala Tyr Gly Trp Glu Trp Pro Leu Asn Glu Asp Gln Val Leu
                885                 890                 895

Glu Arg Leu Leu Ala Leu Asn Leu Glu Arg Cys Pro Ala
            900                 905

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Trp Arg Thr Leu Lys Gly Asp Glu Lys Gly Glu Ser Gln Val Phe Leu
            20                  25                  30

Asp Arg Leu Phe Gln Ala Phe Gly His Ala Gly Tyr Lys Glu Ala Gly
        35                  40                  45

Ala Glu Leu Glu Tyr Arg Val Ala Lys Gln Gly Gly Gly Lys Lys Phe
    50                  55                  60

Ala Asp Leu Leu Trp Arg Pro Arg Val Leu Ile Glu Met Lys Lys Arg
65                  70                  75                  80

Gly Glu Lys Leu Ala Asn His Tyr Gln Gln Ala Phe Asp Tyr Trp Leu
                85                  90                  95

Lys Leu Val Pro Asp Arg Pro Arg Tyr Ala Val Leu Cys Asn Phe Asp
            100                 105                 110

Glu Leu Trp Val Tyr Asp Phe Asn Gln Gln Leu Asp Glu Pro Met Asp
        115                 120                 125

Arg Leu Arg Ile Glu Glu Leu Pro Glu Arg Tyr Thr Val Leu Asn Phe
    130                 135                 140

Met Phe Glu Gln Glu Arg Ala Pro Leu Phe Gly Asn Asn Arg Val Asp
145                 150                 155                 160
```

```
Val Thr Arg Glu Ala Ala Asp Ser Val Ala Lys Val Leu Asn Ser Val
                165                 170                 175

Ile Ala Arg Gly Glu Asp Arg Ala Arg Ala Gln Arg Phe Leu Leu Gln
            180                 185                 190

Cys Val Met Ala Met Phe Ala Glu Asp Phe Glu Leu Ile Pro Arg Gly
        195                 200                 205

Phe Phe Thr Glu Leu Ala Asp Asp Ala Arg Ala Gly Arg Gly Ser Ser
    210                 215                 220

Phe Asp Leu Phe Gly Gly Leu Phe Arg Gln Met Asn Thr Ser Glu Arg
225                 230                 235                 240

Ala Arg Gly Gly Arg Phe Ala Pro Ile Pro Tyr Phe Asn Gly Gly Leu
                245                 250                 255

Phe Arg Ala Val Asp Pro Ile Glu Leu Asn Arg Asp Glu Leu Tyr Leu
            260                 265                 270

Leu His Lys Ala Ala Leu Glu Asn Asn Trp Ala Arg Ile Gln Pro Gln
        275                 280                 285

Ile Phe Gly Val Leu Phe Gln Ser Ser Met Asp Lys Lys Glu Gln His
    290                 295                 300

Ala Lys Gly Ala His Tyr Thr Ser Glu Ala Asp Ile Met Arg Val Val
305                 310                 315                 320

Leu Pro Thr Ile Val Thr Pro Phe Gln Arg Gln Ile Glu Ala Ala Thr
                325                 330                 335

Thr Gln Lys Glu Leu Arg Ala Ile Leu Asp Glu Leu Ala Ser Phe Gln
            340                 345                 350

Val Leu Asp Pro Ala Cys Gly Ser Gly Asn Phe Leu Tyr Val Ala Tyr
        355                 360                 365

Arg Glu Leu Arg Arg Leu Glu Ala Arg Ala Leu Leu Arg Leu Arg Asp
    370                 375                 380

Leu Ser Ala Pro Gly Thr Ala Leu Pro Pro Ala Arg Val Ser Ile Arg
385                 390                 395                 400

Gln Met His Gly Leu Glu Tyr Asp Pro Phe Gly Val Glu Leu Ala Lys
                405                 410                 415
```

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Val Thr Leu Thr Leu Ala Lys Glu Leu Ala Ile Arg Glu Met His Asp
            420                 425                 430

Leu Leu Gly Asn Thr Gly Leu Asp Phe Asp Gln Pro Leu Pro Leu Asp
        435                 440                 445

Asn Leu Asp Asp Arg Ile Val Gln Gly Asp Ala Leu Phe Thr Pro Trp
    450                 455                 460

Pro Arg Val Asp Ala Ile Val Gly Asn Pro Pro Phe Gln Ser Lys Asn
465                 470                 475                 480

Lys Leu Gln Arg Glu Met Gly Ala Ala Tyr Val Lys Lys Leu Arg Ala
                485                 490                 495

His Tyr Pro Asp Val Pro Gly Arg Ala Asp Tyr Cys Val Tyr Trp Ile
            500                 505                 510

Arg Lys Ala His Asp Gln Leu Gly Ser Gly Gln Arg Ala Gly Leu Val
        515                 520                 525

Gly Thr Asn Thr Ile Arg Gln Asn Asp Ser Arg Val Gly Gly Leu Asp
    530                 535                 540

Tyr Val Val Gln His Gly Gly Thr Ile Thr Asp Ala Val Gly Thr Gln
545                 550                 555                 560

Val Trp Ser Gly Asp Ala Ala Val His Val Ser Ile Val Asn Trp Val
                565                 570                 575

Lys Gly Pro Ala Glu Gly Pro Lys His Leu Ala Trp Gln Val Gly Asp
            580                 585                 590

His Arg Thr Ser Pro Trp Gln Ser Thr Glu Leu Pro Val Ile Asn Ser
        595                 600                 605

Ala Leu Ser Ala Gly Thr Asp Val Thr Gln Ala Gln Lys Leu Arg Val
    610                 615                 620

Asn Met Asn Ser Gly Ala Cys Tyr Gln Gly Gln Thr His Gly His Lys
625                 630                 635                 640

Gly Phe Leu Leu Asp Gly Leu Glu Ala Gly Gln Met Leu Ser Ala Glu
                645                 650                 655

Arg Lys Asn Ala Glu Val Ile Phe Pro Tyr Leu Thr Gly Asp Glu Leu
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660 665 670

Leu Arg Thr Ser Pro Pro His Pro Thr Arg Tyr Val Ile Asp Phe Gln
675 680 685

Pro Arg Asp Val Phe Gly Ala Arg Ala Tyr Lys Leu Pro Phe Ala Arg
690 695 700

Ile Glu Arg Glu Val Leu Pro Thr Arg Gln Ala Ala Ala Ala Glu Glu
705 710 715 720

Glu Ala Arg Asn Ala Glu Val Leu Ala Ala Asn Pro Lys Ala Lys Thr
725 730 735

Asn Lys His His Arg Asn Phe Leu Asn Gln Trp Trp Ala Leu Ser Tyr
740 745 750

Gly Arg Ser Glu Met Ile Glu Lys Ile Ser Ser Leu Ser Arg Tyr Ile
755 760 765

Val Cys Ser Arg Val Thr Lys Arg Gln Val Phe Glu Phe Leu Asp Asn
770 775 780

Gly Ile Arg Pro Ser Asp Gly Leu Gln Ile Phe Ala Phe Glu Asp Asp
785 790 795 800

Tyr Ser Phe Gly Val Ile Gln Ser Ser Val His Trp Gln Trp Leu Ile
805 810 815

Ala Arg Gly Gly Thr Leu Thr Ala Arg Leu Met Tyr Thr Ser Asp Thr
820 825 830

Val Phe Asp Thr Phe Pro Trp Pro Asp Pro Thr Leu Ala Gln Val Arg
835 840 845

Ala Val Ala Ala Ala Ala Val Lys Leu Arg Glu Leu Arg Asn Lys Val
850 855 860

Met Arg Glu Gln Gly Trp Ser Leu Arg Asp Leu Tyr Arg Thr Leu Asp
865 870 875 880

Met Pro Gly Lys Asn Pro Leu Arg Asp Ala Gln Glu Arg Leu Asp Ala
885 890 895

Ala Val Ser Ala Ala Tyr Gly Leu Pro Ala Gly Ala Asp Met Leu Asp
900 905 910

Phe Leu Leu Ala Leu Asn Ala Xaa Val Ala Ala Ala Glu Ala Arg Gly
915 920 925

Ala Ala Val Thr Gly Pro Gly Leu Pro Ala Gly Leu Asn Thr Ala Asp
930 935 940

Phe Val Thr Ala Asp Ala Val Arg Pro Leu Gly
945 950 955

<210> 15
<211> 14
<212> PRT
<213> unknown

<220>
<223> first 14 amino terminal residues of MmeI

<400> 15

Ala Leu Ser Trp Asn Glu Ile Arg Arg Lys Ala Ile Glu Phe
1 5 10

<210> 16
<211> 29
<212> PRT
<213> unknown

<220>
<223> first 29 residues of the 25kD peptide

<220>
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<222> (20)..(20)
<223> X = Xaa (any amino acid)

<220>
<221> MISC_FEATURE
<222> (21)..(21)
<223> X = Xaa (any amino acid)

<220>
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<222> (23)..(23)
<223> X = Xaa (any amino acid)

<220>
<221> MISC_FEATURE
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<223> X = Xaa (any amino acid)

<400> 16

Met Lys Ile Ser Asp Glu Phe Gly Asn Tyr Phe Ala Arg Ile Pro Leu
1 5 10 15

Lys Ser Thr Xaa Xaa Ile Xaa Glu Xaa Asn Ala Leu Gln
20 25

<210> 17
<211> 40
<212> PRT
<213> unknown

<220>
<223> first 40 amino acid residues obtained from the 14 kD fragment

<220>
<221> MISC_FEATURE
<222> (36)..(36)
<223> X=Xaa (any amino acid)

<400> 17

Met Asp Ala Lys Lys Arg Arg Asn Leu Gly Ala His Tyr Thr Ser Glu
1 5 10 15

Ala Asn Ile Leu Lys Leu Ile Lys Pro Leu Leu Leu Asp Glu Leu Trp
20 25 30

Val Val Phe Xaa Lys Val Lys Asn
35 40

<210> 18
<211> 25
<212> PRT
<213> unknown

<220>
<223> first 25 residues of the 7.5 kD peptide

<400> 18

Met Lys Ser Arg Gly Lys Asp Leu Asp Lys Ala Tyr Asp Gln Ala Leu
1 5 10 15

Asp Tyr Phe Ser Gly Ile Ala Glu Arg
20 25

<210> 19
<211> 8
<212> PRT
<213> unknown

<220>
<223> 25 kD fragment primer

<400> 19

Asp Glu Phe Gly Asn Tyr Phe Ala
1 5

<210> 20

<211> 20
<212> DNA
<213> unknown

<220>
<223> forward primer

<220>
<221> misc_feature
<222> (3)..(3)
<223> R = A or G

<220>
<221> misc_feature
<222> (6)..(6)
<223> Y = T or C

<220>
<221> misc_feature
<222> (9)..(9)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (12)..(12)
<223> Y = T or C

<220>
<221> misc_feature
<222> (15)..(15)
<223> Y = T or C

<220>
<221> misc_feature
<222> (18)..(18)
<223> Y = T or C

<400> 20
garttyggna aytayttygc 20

<210> 21
<211> 20
<212> DNA
<213> unknown

<220>
<223> reverse primer

<220>
<221> misc_feature
<222> (3)..(3)
<223> R = A or G

<220>
<221> misc_feature
<222> (6)..(6)
<223> R = A or G

<220>
<221> misc_feature

<222> (9)..(9)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (12)..(12)
<223> R = A or G

<220>
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<222> (15)..(15)
<223> Y = T or C

<220>
<221> misc_feature
<222> (18)..(18)
<223> R = A or G

<400> 21
aartarttnc craaytcrtc 20

<210> 22
<211> 6
<212> PRT
<213> unknown

<220>
<223> 14 kD fragment primer

<400> 22

Met Asp Ala Lys Lys Arg
1 5

<210> 23
<211> 17
<212> DNA
<213> unknown

<220>
<223> forward primer

<220>
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<222> (6)..(6)
<223> Y = T or C

<220>
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<222> (9)..(9)
<223> n is a, c, g, or t

<220>
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<222> (12)..(12)
<223> R = A or G

<220>
<221> misc_feature
<222> (15)..(15)

<223> R = A or G

<400> 23
atggaygcna araarcg 17

<210> 24
<211> 17
<212> DNA
<213> unknown

<220>
<223> reverse primer

<220>
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<222> (6)..(6)
<223> Y = T or C

<220>
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<222> (9)..(9)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (12)..(12)
<223> R = A or G

<220>
<221> misc_feature
<222> (15)..(15)
<223> R = A or G

<400> 24
atggaygcna araarag 17

<210> 25
<211> 20
<212> DNA
<213> unknown

<220>
<223> reverse primer

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<222> (3)..(3)
<223> n is a, c, g, or t

<220>
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<222> (6)..(6)
<223> Y = T or C

<220>
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<222> (9)..(9)
<223> Y = T or C

<220>
<221> misc_feature
<222> (12)..(12)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (15)..(15)
<223> R = A or G

<400> 25
cgncgyttyt tngcrtccat 20

<210> 26
<211> 7
<212> PRT
<213> unknown

<220>
<223> 7.5 kD fragment primer

<400> 26

Asp Lys Ala Tyr Asp Gln Ala
1 5

<210> 27
<211> 20
<212> DNA
<213> unknown

<220>
<223> forward primer

<220>
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<222> (3)..(3)
<223> Y = T or C

<220>
<221> misc_feature
<222> (6)..(6)
<223> R = A or G

<220>
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<222> (9)..(9)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (11)..(11)
<223> Y = T or C

<220>
<221> misc_feature
<222> (14)..(14)
<223> Y = T or C

<220>

<221> misc_feature
<222> (17)..(17)
<223> R = A or G

<400> 27
gayaargcnt aygaycargc 20

<210> 28
<211> 20
<212> DNA
<213> unknown

<220>
<223> reverse primer

<220>
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<222> (3)..(3)
<223> Y = T or C

<220>
<221> misc_feature
<222> (6)..(6)
<223> R = A or G

<220>
<221> misc_feature
<222> (9)..(9)
<223> R = A or G

<220>
<221> misc_feature
<222> (12)..(12)
<223> n is a, c, g, or t

<220>
<221> misc_feature
<222> (15)..(15)
<223> Y = T or C

<220>
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<222> (18)..(18)
<223> R = A or G

<400> 28
gcytgrtcrt angcyttrtc 20

<210> 29
<211> 26
<212> DNA
<213> unknown

<220>
<223> primer IP 1

<400> 29
gttggatccc gcacagattg ctcagg 26

<210> 30
<211> 30
<212> DNA
<213> unknown

<220>
<223> primer IP 2

<400> 30
gttggatcct acgttaatct gaataagatg 30

<210> 31
<211> 28
<212> DNA
<213> unknown

<220>
<223> primer IP 3

<400> 31
gttggatcct gttaatctga aacgctgg 28

<210> 32
<211> 29
<212> DNA
<213> unknown

<220>
<223> primer IP 4

<400> 32
gttggatcct tataccaaaa tgtgaggtc 29

<210> 33
<211> 20
<212> DNA
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<220>
<223> primer IP 5

<400> 33
ttcagaaata cgagcgatgc 20

<210> 34
<211> 20
<212> DNA
<213> unknown

<220>
<223> primer IP 6

<400> 34
gtcaagccat aaacaccatc 20

<210> 35
<211> 20
<212> DNA

<213> unknown

<220>
<223> primer IP 7

<400> 35
gagggtcaga aaggaagctg 20

<210> 36
<211> 20
<212> DNA
<213> unknown

<220>
<223> primer IP 8

<400> 36
gtccaactaa ccctttatgg 20

<210> 37
<211> 20
<212> DNA
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<220>
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<400> 37
ttcctagtgc tgaacctttg 20

<210> 38
<211> 20
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<220>
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<400> 38
gttgcgttac ttgaaatgac 20

<210> 39
<211> 20
<212> DNA
<213> unknown

<220>
<223> primer IP 11

<400> 39
ccaaaatgga acttgtttcg 20

<210> 40
<211> 20
<212> DNA
<213> unknown

<220>

<223> primer IP 12

<400> 40
gtgagtgcgc cctgaattag 20

<210> 41
<211> 21
<212> DNA
<213> unknown

<220>
<223> primer S1

<400> 41
gcttcatttc atcctctgtg c 21

<210> 42
<211> 21
<212> DNA
<213> unknown

<220>
<223> primer S2

<400> 42
taaccgccaa aattaatcgt g 21

<210> 43
<211> 20
<212> DNA
<213> unknown

<220>
<223> primer S3

<400> 43
ccactattca ttacaacacc 20

<210> 44
<211> 43
<212> DNA
<213> unknown

<220>
<223> 20 nucleotides that matched the M. methyltrophus DNA sequence

<400> 44
gttctgcagt taaggataac atatggcttt aagctggaac gag 43

<210> 45
<211> 37
<212> DNA
<213> unknown

<220>
<223> 22 nucleotides that matched the M. methylotrophus DNA sequence

<400> 45

gttggatccg tcgacattaa ttaatttttg cccttag 37

<210> 46
<211> 48
<212> DNA
<213> unknown

<220>
<223> oligonucleotide 1

<400> 46
gtttgaagac tccgacgcga tggccagcga tcggcgcctc agcttttg 48

<210> 47
<211> 48
<212> DNA
<213> unknown

<220>
<223> oligonucleotide 2

<400> 47
caaaagctga ggcgccgatc gctggccatc gcgtcggagt cttcaaac 48

<210> 48
<211> 48
<212> DNA
<213> unknown

<220>
<223> oligonucleotide 3

<220>
<221> misc_feature
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<223> A = 6-methyladenine

<400> 48
gtttgaagac tccgacgcga tggccagcga tcggcgcctc agcttttg 48

<210> 49
<211> 48
<212> DNA
<213> unknown

<220>
<223> oligonucleotide 4

<220>
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<222> (38)..(38)
<223> A = 6-methyladenine

<400> 49
caaaagctga ggcgccgatc gctggccatc gcgtcggagt cttcaaac 48

<210> 50
<211> 8
<212> PRT
<213> unknown

<220>
<223> single internal CnBr digestion fragment

<400> 50

Gly Arg Gly Arg Gly Val Gly Val
1 5